REMARKS

Claims 1, 4, 6-9, 13, 18, 19, 23, 24, 28-31, and 36-56 are pending. Claims 36-50 are withdrawn from consideration. By virtue of this response, claims 1 and 6 are amended; and claim 51 is cancelled. The nucleotide sequences (SEQ ID NOS:185-188) recited in claim 1 as amended correspond to GenBank accession numbers L32836, M15185, M61831, and M61832. Claim 6 is amended to incorporate the feature in claim 51. Accordingly, claims 1, 4, 6-9, 13, 18, 19, 23, 24, 28-31, and 52-56 are under consideration.

The specification is amended to incorporate nucleotide sequences corresponding to GenBank accession numbers L32836, M15185, M61831, and M61832. Based on the information from www.ncbi.nlm.nih.gov, the GenBank entry for L32836 was last modified on July 25, 1995; the GenBank entry for M15185 was last modified on October 4, 1994; the GenBank entry for M61831 was last modified on November 1, 1994; and the GenBank entry for M61832 was last modified on November 1, 1994. Thus, the sequences recited in GenBank entries downloaded at the time as indicated in the references submitted herein as Exhibits A-D of Yuan Declaration are the same as the sequences recited in GenBank entries at the priority date (July 6, 1999) of the present application. A Declaration executed by the applicant, Dr. Chong-Sheng Yuan, is submitted with this response. The Declaration states that the amendatory material consists of the same material incorporated by reference in the present application. Accordingly, no new matter has been added. Submitted herewith is a Substitute Sequence Listing (paper copy and computer readable version) including the previously submitted SEQ ID NOS. 1-184 and the new SEQ ID NOS. 185-188.

The amendments are made solely to promote prosecution without prejudice or disclaimer of any previously claimed subject matter. With respect to all amendments and cancelled claims, Applicant has not dedicated or abandoned any unclaimed subject matter and moreover has not acquiesced to any rejections and/or objections made by the Patent Office. Applicant expressly reserves the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

Claim rejections under 35 U.S.C. §112, second paragraph

Claims 1, 4, 8-9, 13, 18-19, 23-24, and 28-31 are rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner states that entries in GenBank can maintain the accession number even if there are modifications in the sequence, and thus, the recitation of accession numbers render the instant claim indefinite in view of the fact that the sequence in the accession number may vary.

Without acquiescence to the rejection, Applicant has amended claim 1 to recite nucleotide sequences (SEQ ID NOS:185, 186, 187, and 188) that correspond to the GenBank accession numbers L32836, M15185, M61831, and M61832, respectively. Accordingly, claim 1 as amended is not indefinite.

In view of the above, Applicant respectfully requests that the rejection be withdrawn.

Claim rejections under 35 U.S.C. §112, first paragraph

A. Written Description

Claims 1, 4, 6, 8-9, 13, 18-19, 23-24, 28-31, and 52-56 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement.

With respect to claims 1, 4, 8-9, 18-19, 23-24, and 28-31, the Examiner states that some of the GenBank entries disclose ESTs encoding partial proteins and SAH hydrolases of substantially different sizes from that of SEQ ID NO:1 (432 amino acids). The Examiner further states that while the specification may provide some guidance as to which amino acids can be mutated to obtain the desired functional properties if there is a significant level of homology between the exemplary mouse/human SAH hydrolases of the specification and the SAH hydrolase to be mutated, in the

instant case, it is unclear as to how the teachings of the specification adequately describe the mutation of an SAH hydrolase of any size. The Examiner states that based on the mutations disclosed for a 432 amino acid SAH hydrolase without an additional structural/functional correlation sufficient for one skill in the art to identify those amino acids which, when mutated, would provide an SAH hydrolase having the recited functional characteristics.

Without acquiescence to the rejection and in the interest of expediting prosecution, Applicant has amended claim 1 to recite a mouse (L32836), a rat (M15185), and two human (M61831 and M61832) nucleotide sequences which encode full length SAH hydrolase. As shown in Exhibit 2, the mouse, rat and human SAH hydrolases encoded by these nucleotide sequences all have 430 amino acids, and amino acid sequences between the mouse, rat, and human SAH hydrolases are highly homologous. Applicant notes that the amino acid sequence in SEQ ID NO:1 is the same amino acid sequence encoded by the nucleotide sequence having GenBank accession number M61831. In view of the extremely high level of homology between these sequences, Applicant respectfully submits that the claims as amended are supported by structural features and by functional characteristics coupled with a known correlation between function and structure; and one skilled in the art can mutate any of these three genes to obtain mutant SAH hydrolase having binding affinity for Hcy, SAH or adenosine but having attenuated catalytic activity as claimed based on their homology to amino acid residues in SEQ ID NO:1 that are directly interacting with the substrate and coenzyme, and amino acid residues that are adjacent to amino acid residues that are directly interacting with the substrate and coenzyme. Accordingly, Applicant respectfully submits that claims 1, 4, 8-9, 18-19, 23-24, and 28-31 as amended satisfy the written description requirement.

With respect to claims 6 and 52-56, the Examiner states that the claims encompass the use of mutants of any human SAH hydrolase, including unknown human SAH hydrolase. The Examiner alleges that several human SAH hydrolases of different sizes exist, citing several references. The Examiner further alleges that the specification fails to disclose which structural elements of SEQ ID NO:1 would be required in any human SAH hydrolase or how SEQ ID NO:1 correlates with the structures of all possible human SAH hydrolases.

Without acquiescence to the rejection and in the interest of expediting prosecution, Applicant has amended claim 6 to recite that the human SAH hydrolase comprises the amino acid sequence set forth in SEQ ID NO:1, which is the feature in claim 51. Applicant respectfully note that claim 51 is not rejected by the Examiner. Accordingly, Applicant respectfully submit that claims 6 and 52-56 as amended satisfy the written description requirement.

In view of the above, Applicant respectfully submits that the written description requirement has been met in view of the claim amendment, and withdrawal of this rejection is respectfully requested.

B. Enablement

Claims 1, 4, 6, 8-9, 13, 18-19, 23-24, 28-31, and 52-56 are rejected under 35 U.S.C. §112, first paragraph. The Examiner alleges that while being enabling for a method for assaying Hcy, SAH, or adenosine with a mutant SAH hydrolase wherein said SAH hydrolase comprises SEQ ID NO:1 and also has specific substitutions at the positions recited in claim 7, and those positions disclosed in the specification, wherein said mutant has the specific functional characteristics recited, does not provide enablement for method for assaying Hcy, SAH, or adenosine with a mutant SAH hydrolase wherein said mutant SAH hydrolase is derived from (1) any human SAH hydrolase, (2) any SAH hydrolase where a substantial portion of its structure has not been disclosed, or (3) any SAH hydrolase where its complete structure is disclosed which does not have substantial structural homology to the mouse and human species disclosed in the specification. The Examiner states that the specification does not enable any person of skill in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The Examiner further states that the specification does not provide any information as to which additional structural elements are required in those ESTs recited in claim 1 such that they would encode a protein having SAH hydrolase activity. The Examiner further states that while the specification may provide some guidance as to which amino acid can be mutated to obtain the desired functional properties if there is a significant level of homology between the mouse/human SAH hydrolases of the specification and the SAH hydrolase to be mutated, there is no teaching in

the specification regarding how to mutate an SAH hydrolase of any size, such as that encoded by the sequence of GenBank entry AF129871, which is almost a quarter of the size of that of SEQ ID NO:1, based on the mutations disclosed for a 432 amino acid SAH hydrolase without an additional structural/functional correlation sufficient for one of skill in the art to identify those amino acids which when mutated would provide an SAH hydrolase having the recited functional characteristics. The Examiner further states that the specification fails to disclose which structural elements of SEQ ID NO:1 would be required in any human SAH hydrolase or how SEQ ID NO:1 correlates with the structures of all possible human SAH hydrolase.

Applicant respectfully notes that claim 1 has been amended to recite specific nucleotide sequences encoding the mouse, rat, and human SAH hydrolases, and claim 6 has been amended to recite that the human SAH hydrolase comprising the amino acid sequence set forth in SEQ ID NO:1. As shown in Exhibit 2, amino acid sequences are highly homologous between the mouse, rat, and human SAH hydrolases recited in the claims. One skilled in the art could apply the teachings of the specification to mutate these genes to obtain mutant SAH hydrolase having binding affinity for Hcy, SAH or adenosine but having attenuated catalytic activity as claimed based on their homology to amino acid residues (in SEQ ID NO:1) that are directly interacting with and amino acid residues (in SEQ ID NO:1) that are adjacent to amino acid resides that are directly interacting with the substrate and coenzyme without undue experimentation.

In view of the above, Applicant respectfully submits that claims as amended are enabled. Applicant respectfully requests that reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph.

Claim rejections under 35 U.S.C. §102

Claims 6 and 51 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Yuan et al. The Examiner states that Yuan et al. teach a human placental SAH hydrolase which comprises the amino acid sequence as set forth in SEQ ID NO:1 and that modification of three of the ten cysteine residues per enzyme subunit resulted in complete inactivation of the enzyme. The

Examiner alleges that the assay of mutant enzyme described on page 28010 of Yuan et al. anticipates the instant claims as the detection of binding steps of the mutant SAH hydrolase with Hcy, SAH, or adenosine in a sample as claimed herein is inherent in the detecting of product step by the Yuan et al.

Applicant respectfully traverses this rejection.

Applicant notes that claim 6 has been amended to incorporate the feature in claim 51, and claim 51 has been cancelled. Applicant respectfully submits that claim 6 as amended is not anticipated by Yuan et al. MPEP §2131 provides that a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described in a single prior art reference. Applicant notes that claim 6 recites a step of detecting binding between Hcy, SAH or adenosine with the mutant SAH hydrolase, whereby the presence or amount of Hcy, SAH or adenosine in the sample is assessed. Yuan et al. teach an assay of determining SAH hydrolase activity by measuring the rate of formation of AdoHcy from Ado and Hcy using HPLC, or in the hydrolytic direction, by measuring the rate of the product (Hcy) formed by reaction with DTNB. See, Yuan et al., page 28010, left column, last two paragraphs. Yuan et al. do not teach or suggest detecting binding between Hcy, SAH or adenosine with the mutant SAH hydrolase in order to assess the presence or amount of Hcy, SAH or adenosine in the sample. Thus, the detecting step recited in claim 6 is not inherent in the assay described in Yuan et al. Since Yuan et al. do not teach or suggest detecting binding between Hcy, SAH or adenosine for assessing the presence or amount of Hcy, SAH or adenosine in the sample, Yuan et al. do not anticipate claim 6.

Applicants respectfully request that the rejection under 35 U.S.C. §102(b) be withdrawn.

Double patenting

Claims 6 and 51-56 are rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentably over claims 1-16 of U.S. Patent No. 6376210.

Applicant reiterates that this issue will be addressed when other rejections are withdrawn.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 466992000221. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

By _____

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